REMARKS

Claims 1, 4-6, and 9-47 are currently pending is this application. Claims 11-22, 25-34, and 38-47 have been withdrawn due to restriction requirement. Claims 2, 3, 7, and 8 have been canceled. Claim 1 has been amended to include the subject matter of canceled claims 3and 8. Claim 4 has been amended to provide proper antecedent basis. No new matter has been added.

These papers are filed in response to the Advisory Action mailed June 1, 2011. Applicants appreciate and acknowledge the withdrawal of the rejection of claims 8, 35 and 37 under 35 U.S.C. 103(a) as allegedly being obvious over the combination of Chen and Lerner as evident by Lamosa and further in view of Adusumili et al. (US 2004/0037879).

Applicants file herewith a Request for Continued Examination.

Claim Rejections -35 USC 3 103

Claims 1-10, 23-24, 35-37 are rejected under 35 U.S.C. 103(a) as allegedly being obvious over Chen et al. (US 2003/0068376) in view of Lerner et al. (US 6,197,331), as evident by the article by Lamosa et al. ("Design of Microencapsulated Chitosan Microspheres for Colonic Drug Delivery"). Applicants traverse this rejection.

One-skilled in the art would not combine the cited references. Chen is directed to "an intraoral ***quick-dissolving film*** which is applied lingually. The dosage form is applied to the tongue . . . and rapidly disintegrates, dissolves and releases [nicotine]." (Chen, paragraph [0051]) (emphasis added). As recognized by the Action, Chen does not teach the use of enteric polymers for its film. Rather, the films in Chen comprise a non-microbial hydrocolloid and nicotine. Chen describes this non-microbial hydrocolloid as water soluble and non-gelling natural gums or derivatives thereof, water soluble and non-gelling polypeptides, and water soluble synthetic polysaccharides. There is no suggestion in Chen that these water soluble components can or should be replaced with enteric polymers or that enteric polymers would produce the described quick-dissolving film. The quick-dissolving film of Chen provides for "a relatively rapid initial increase in blood nicotine concentration [that] simulate[s] the pattern obtained by smoking a cigarette or taking a nasal spray." (Chen, paragraph [0052]).

Lerner is directed to an oral patch that "adhere[s] to hard dental surfaces, such as teeth and dentures." (Lerner, col. 1, lines 11-12) (emphasis added). The oral patch is designed to ***remain on the tooth*** or denture for a period of time and provide ***controlled or sustained***

release of pharmaceutical agents to the patent. Although Lerner refers to certain enteric Eudragit® polymers[1] as suitable polymers for release layers and/or adhesive layers, there is no discussion of these polymers imparting "quick dissolving" characteristics on the oral patch. This lack of teaching is consistent with the understanding of one skilled in the art with respect to enteric coatings – enteric polymers are useful for delayed release of an active agent until a particular dosage form reaches the intestine. Lerner repeatedly refers to controlled or sustained release characteristics of the oral patch. This is consistent with Lerner's use of the enteric polymers to enhance mucoadhesion to immobilize the device in the oral cavity and regulate its release mechanisms, such as erosion and diffusion, for a prolonged period of time. Additionally, Lerner further distinguishes itself from quick dissolving films, like those disclosed in Chen. Lerner states that a significant advantage of its "oral patch" over films is that the oral patch provides for greater adhesion than films, resulting in ***treatment for longer periods of time*** (Lerner, col. 10, lines 17-26).

The Advisory Action dated June 1, 2011, states:

> it is argued that the present claims are not directed to any method of application of the orally dissolvable film, rather directed to a product that dissolves in the oral cavity . . . It is noted that the features upon which applicant relies (i.e. site of application and speed of dissolution of the film) is not recited in the rejected claims

(Advisory Action, page 3). Applicants assert that the distinctions referred to by the Examiner need not appear in the present claims to show that one skilled in the art would not be motivated to combine Chen, directed to a quick dissolving film, with Lerner directed to controlled or sustained release oral patch.

Additionally, there is no suggestion or motivation to combine Chen with Lerner because combination of these references would result in a nicotine film that would be unsatisfactory for its intended purpose. Indeed, combination of the nicotine salts disclosed in Chen with the enteric polymers disclosed in Lerner would not result in a film that would dissolve in the oral cavity to release nicotine completely. The nicotine disclosed in Chen is limited to "nicotine base and its salts." The enteric polymers recited in Lerner require a specific pH to be soluble. For example, Eudragit L100 will only dissolve at a pH above 5.5.

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[1] Contrary to the Action's statement that "applicants themselves admit, Lerner teaches neutral enteric polymers" 2/8/2011 Action, page 17), Applications do not admit that Lerner teaches neutral enteric polymers.

If one were to combine the nicotine salts disclosed in Chen with these polymers directly, the acidic counter ions associated with the nicotine salts would lower the pH of the formulation and not provide the pH needed to dissolve the film. This makes it inoperable for its intended purpose, which is to release nicotine rapidly into the oral cavity of a user when administered on the tongue.

Furthermore, even if one were motivated to combine the references, combination of these references does not teach the claimed invention. Independent claim 1 has been amended to recite a ***nicotine oil***. As recognized by the Examiner, Chen does not disclose nicotine oil in its compositions. Chen, on the contrary, is limited to "nicotine base and its salts." The Action, however, states that "regarding nicotine oil . . . , applicants failed to show unexpected results obtained from nicotine oil . . . over the use of nicotine salts disclosed by Chen et al." (Office Action, p. 7). As mentioned above, however, nicotine salts are not suitable for use in orally dissolvable films containing the enteric/acidic polymers of the present invention because the solubility of the enteric polymer is pH-dependent.

Applicants have recognized that the use of a neutral nicotine, such as a nicotine oil, overcomes the problems associated with the decrease in pH from the nicotine salts. There are, however, problems associated with using neutral nicotine oils in films. When neutral, nicotine oil is quite volatile and this is particularly an issue when forming nicotine-containing films using a solvent coating process. For example, during the drying process to remove solvents, much of the neutral nicotine evaporates from the film, resulting in a film containing much less nicotine than desired. In addition, the film is susceptible to additional loss of nicotine during storage. To overcome these problems, Applicants recognized the importance of partially pre-neutralizing Eudragit polymer using a neutralizing agent. The benefits are four-fold. First, the nicotine exists as a monocation at the formulated pH (6 to 6.5) which is no longer volatile. Second, the formulated pH which only partially pre-neutralizes the enteric polymer, allows the polymer to serve as a polymeric ligand to immobilize the nicotine by forming an ionic complex between the nicotine and the partially pre-neutralized enteric polymer to prevent it from escaping with solvent (water/ethanol) during the drying process. Third, the nicotine and Eudragit ionic and polymeric complex prevent the physical immigration of nicotine during storage and stability study. Fourth, the formulated pH which partially pre-neutralizes Eudragit, provides a film that keeps its integrity when handled and dissolves rapidly in a small volume of saliva.

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. An indication of allowability of the claimed design is requested respectfully. Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned attorney at the number below.

Respectfully submitted,

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